

(b) a sequence hybridising with all or part of the complementary strand of sequence SEQ ID

NO:3.--

Page 4, paragraph beginning on line 13, delete in its entirety and insert therefor the following new paragraph.

a2 --More preferably, the nucleic acid of the invention comprises all or a portion of sequence SEQ ID NO:3.--

Page 4, paragraph beginning on line 29 and ending on page 5, line 7, delete in its entirety and insert therefor the following new paragraph.

a3 --The term "portion" or "fragment" of nucleic acid means any nucleic acid comprising at least a portion of the sequence under consideration (for example sequence SEQ ID NO:3 and which retains a transcriptional promoter activity. The sequence portion advantageously contains at least 50 bp, more preferably at least 100 bp. These "portions" can readily be generated using conventional molecular biological techniques, either by enzymatic cleavage and digestion from the fragments describes, or by synthesis using nucleic acid synthesisers.--

Page 5, paragraph beginning at line 4, delete in its entirety and insert therefor the following new paragraph.

a4 --The term "hybridising" as used in the present invention means any hybridisation under normal conditions, which may be stringent or non stringent, as defined below. An example of stringent hybridisation conditions is: Hybridisation at 42°C, 50% formamide, 5 X SSC, 1 X Denardt; Wash at 65°C in 0.1 X SSC, 0.1% SDS. Non stringent conditions are: Hybridisation at 37°C, 40% formamide, 5 X SSC, 1X Denardt; Wash at 50°C in 1 X SSC, 0.1% SDS. Stringent conditions are particularly suitable when the nucleic acids are present in small quantities and/or are in purified form. Non stringent conditions are more suitable when the nucleic acid present in large quantities and are significantly represented in the

sample. Advantageously, "hybridising" sequences are sequences which hybridise under stringent conditions, and which thus have a high degree of structural homology with the sequence under consideration (for example SEQ ID [n°] NO:2) or its fragments. Further, hybridising sequences can include a region enabling hybridisation and a contiguous region which is not hybridising, but corresponding to flanking regions.--

Page 6, paragraph beginning at line 17, delete in its entirety and insert therefor the following new paragraph.

CS --To this end, the inventors have also demonstrated the existence in the identified gene of such a secretion signal, which is particularly active in bacteria from the genus *Clostridium*. This signal is represented by residues 268-357 in sequence SEQ ID NO:1, and separately in SEQ ID NO:4. This signal, or any variant or active fragment thereof, constitutes an advantageous embodiment of the invention.--

Page 14, paragraph beginning at line 29, delete in its entirety and insert therefor the following new paragraph.

96 --Figure 8: Hydrophobicity profile for beta 2 toxin (SEQ ID NO:2).--

Page 15, paragraph beginning at line 1, delete in its entirety and insert therefor the following new paragraph.

--SEQ ID NO:1: Gene sequence for beta 2 toxin of type C *Clostridium perfringens*.

CS SEQ ID NO:3: Sequence for beta 2 toxin gene promoter of type C *Clostridium perfringens*.

CS SEQ ID NO:4: Sequence for secretion signal of beta 2 toxin gene of type C *Clostridium perfringens*.

SEQ ID NO:6: Sequence of primer P318.

SEQ ID NO:7: Sequence of primer P292.--

Page 16, lines 29 and 30, delete in their entirety and insert therefor:

as --P318: 5'-GAAATGTTTACAACGTATTAATATCGTAG-3' (SEQ ID NO:6)

P292: 5'-TCAAGTTTGTACATGGGATGATG-3' (SEQ ID NO:7)--

Page 17, paragraph beginning at line 8, delete in its entirety and insert therefor the following new paragraph:

ca --The sequence obtained in Example A (SEQ ID NO:1) comprises an open reading frame coding for the mature beta 2 toxin (residues 358 to 1122), and regulating or addressing regions located at the 5' and 3' end. The promoter region in the gene of the beta 2 toxin of type C *Clostridium perfringens* can be pinpointed on this sequence as comprising residues 1 to 267. This promoter sequence in the beta 2 toxin gene of type C *Clostridium perfringens* is shown separately in sequence SEQ ID NO:3. This sequence includes a consensus ribosome binding site (GGGGGG) located 7 nucleotides upstream of the start codon ATG, i.e., at positions 255-260 in sequence SEQ ID NO:3.--

Page 17, paragraph beginning at line 17, delete in its entirety and insert therefor the following new paragraph.

ca This region, or any fragment or variation thereof, can be isolated from samples of *Clostridium* nucleic acids using suitable probes (for example corresponding to sequence SEQ ID NO:3 or a fragment thereof) or by chemical synthesis, or by enzymatic digestion from the plasmids of the invention, in particular the plasmid pMRP268, deposited on 8th August 1997 at the Collection of the Institut Pasteur (CNCM: Collection Nationale de Cultures de Microorganismes), accession number I-1911.--

Page 18, paragraph beginning at line 5, delete in its entirety and insert therefor the following new paragraph.

Q11
--In addition to an open reading frame and transcription regulation regions (Example B), the sequence obtained in Example A (SEQ ID NO:1) also comprises addressing signals enabling a protein or peptide to be directed during synthesis towards the host cell secretion routes. The addressing region (secretion signal peptide) of the beta 2 toxin gene of type C *Clostridium perfringens* can be seen in sequence SEQ ID NO:1 as including residues 268 to 357. This signal peptide sequence in sequence SEQ ID NO:4. This region codes for 30 amino acids, comprising a hydrophobic region (residues 6-26), probably forming a transmembrane domain, bordered by charged amino acids (Lys2, Lys3, Lys7 and Lys27). Further, the junction region between this signal sequence and the mature protein (Ala30-Lys31) corresponds to the (Ala-X) cleavage site of the major portion of bacterial signal peptidases.--

Page 18, paragraph beginning at line 18, delete in its entirety and insert therefor the following new paragraph.

Q12
--This region, or any fragment or variant thereof, can be isolated from samples of *Clostridium* nucleic acids using suitable probes (for example corresponding to sequence SEQ ID NO:4 or a fragment thereof) or by chemical synthesis, or by enzymatic digestion from plasmids of the invention, in particular plasmid pMRP268, deposited on 8th August 1997 in the Institut Pasteur collection (CNCM), accession number I-1911.--

Q13
Page 28, after the last line, beginning on a new page, please insert the attached Sequence Listing.

IN THE CLAIMS

Please amend the claims as follows:

Q14
--1. (Amended) A nucleic acid ^{wherein} ~~characterized in that~~ it has a transcriptional promoter activity and in that ~~it~~ comprises: